NIST Develops Reference Methods and Materials for the Determination of Hormones in Human Serum

Many life functions are regulated by hormones. When hormone levels deviate from the norm, serious health consequences may result. Timely and effective treatments require accurate diagnoses of hormone levels. NIST is developing new reference methods and reference materials to support accuracy and traceability for clinical laboratory measurements of non-steroid hormones related to thyroid function and other metabolic processes

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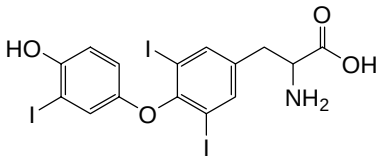
NIST is developing reference methods and Standard Reference Materials (SRMs) to support accuracy and traceability for hormone assays. A suite of reference methods, based on liquid chromatography and mass spectrometry (LC/MS and LC/MS/MS), has now been developed for estradiol-17β [1], testosterone, cortisol, progesterone, thyroxine (T4), and triiodothyronine (T3).

T3 and T4 are hormones produced by the thyroid gland that regulate many cellular functions including carbohydrate metabolism and protein synthesis. Both elevated and decreased thyroid output of these hormones are relatively common conditions. Reference methods for measurement of these hormones in serum have been developed at NIST [2,3] and will be utilized for certification of SRM 971.



T3

A reference method for cortisol has also been developed and published [4]. Cortisol is a hormone produced by the adrenal gland. Measurement of cortisol levels in serum can be used to diagnose problems in the adrenal or pituitary gland, as well as other disorders. Previous experience at NIST and at other laboratories indicated that routine clinical measurements overestimate the cortisol present in serum by 25% to 50% when compared to isotope dilution (ID) MS methods.

Reference method development was recently completed and the method published for progesterone [5]. Progesterone is found at low levels in premenopausal adult women and very low levels in adult men, but levels in women rise significantly during pregnancy. The accuracy of the new isotope dilution LC/MS/MS method for progesterone was established by comparing the results obtained by LC/MS/MS for a Certified Reference Material (CRM) to those obtained by a gas chromatography/mass spectrometry (GC/MS) reference method.

These reference methods are being applied to the certification of a new Standard Reference Material, SRM 971 Hormones in Human Serum. The SRM consists of two serum pools, one from normal adult males and one from normal, premenopausal adult females. Measurements for cortisol and progesterone are completed, and the results will be combined with results from two collaborating laboratories to assign certified values for these two hormones. Measurements for the remaining hormones will be completed in FY07.

Improving the accuracy of clinical assays for hormones will improve diagnoses and result in earlier treatments. The new methods and the SRM will help improve accuracy of these assays and will also provide high-order reference systems for traceability.

Publications:

1. Tai, S.S-C. and Welch, M.J., ***"Development and Evaluation of a Reference Measurement Procedure for the Determination of Estradiol-17β in Human Serum Using ID-LC/MS/MS,"*** Anal. Chem. 77, 6359-6363 (2005).

2. Tai, S.S-C., Bunk, D.M., White V, E., and Welch, M.J., ***"Development and Evaluation of a Reference Measurement Procedure for the Determination of Total 3,3',5-Triiodothyronine in Human Serum Using ID-LC/MS/MS,"*** Anal. Chem. 76, 5092-5096 (2004).

3. Tai, S.S-C., Sniegoski, L.T., and Welch, M.J***., "Determination of Thyroxine in Human Serum by ID-LC/MS with Electrospray Ionization,"*** Clin. Chem. 48, 637-642 (2002).

4. Tai, S.S-C. and Welch, M.J., ***"Development and Evaluation of a Candidate Reference Method for the Determination of Total Cortisol in Human Serum Using ID-LC/MS and LC/MS/MS,"*** Anal. Chem. 76, 1008-1014 (2004).

5. Tai, S.S.-C., Xu, B., and Welch, M.J***., "Development and Evaluation of a Candidate Reference Measurement Procedure for the Determination of Progesterone in Human Serum Using ID-LC/MS/MS,"*** Anal. Chem. 78, 6628-6633 (2006).